



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/US99/25737</p> <p>(22) International Filing Date: 1 November 1999 (01.11.99)</p> <p>(30) Priority Data: 60/106,732 2 November 1998 (02.11.98) US</p> <p>(71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; Bethesda, MD 20892 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): RYBAK, Susanna, M. [US/US]; 7411 B Round Hill Road, Frederick, MD 21702 (US). NEWTON, Dianne, L. [US/US]; 15904 New Bedford Drive, Rockville, MD 20855 (US).</p> <p>(74) Agents: WEBER, Kenneth, A. et al.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).</p>			<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
(54) Title: SELECTIVE TOXICITY OF AMINO-TERMINAL MODIFIED RNASE A SUPERFAMILY POLYPEPTIDES			
(57) Abstract			
<p>This invention provides RNase A superfamily polypeptides with modified amino terminal which can be used to selectively kill target Kaposi's sarcoma cells, neoplastic endothelial cells, and non-neoplastic endothelial cells. In certain embodiments of the invention, the amino terminal modification consists of an addition of 4 amino acid sequence consisting of the SLHV sequence at position -4 to -1 to the eosinophil derived neurotoxin protein. The amino terminal addition is capable of directing the claimed RNase A superfamily polypeptides to proliferating endothelial cells, such as Kaposi's sarcoma cells, and selectively killing these cells.</p>			

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/25737

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07K 5/00; A61K 38/00

US CL :514/12; 530/324

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/12; 530/324

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 99/01152 A1 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA, REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES) 14 January 1999, see SEQ ID No. 10 and abstract.	1-5,8-14,21
X,P	WO 99/01020 A2 (HUMAN GENOME SCIENCES, INC.) 14 January 1999, see pages 5-6.	1-6,8-16,19-21
X	CUBO, M. T. et al. Molecular Characterization and Regulation of the Rhizosphere-Expressed Genes rhiABCR That Can Influence Nodulation by Rhizobium leguminosarum Biovar viciae. J. Bacteriology. June 1992, Vol. 174, No. 12, pages 4026-4035, see Figure 3.	1-6,8-14,21

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ROSENBERG, H. F. et al. Rapid evolution of a unique family of primate ribonuclease genes. Nature Genetics. June 1995, Vol. 10, pages 219-223, see Figure 2-sequence called oECP.	1-5,8-14,21